REMARKS

Claims 1, 5-7, 12, 21, and 26 have been amended. Claims 3, 4, 9, 10, 24, and 25 have been canceled without prejudice. Upon entry of this amendment, claims 1, 2, 5-8, 11, 12, 21, 23, 26, and 27, will be pending and under examination.

Claims 1, 7, and 21 have been amended to delete the phrase "or a fragment thereof comprising at least 10 amino acids of the sequence" and to replace "90%" with "95%." Claims 1, 7, and 21 have also been amended to replace the term "analog" with "agonist," for consistency with the use of the term "agonist" elsewhere in the claims. Claims 5, 11, and 26, have been amended to replace "95%" with "98%." Claims 6, 12, and 27 have been amended to replace "14" with "10." Support for these amendments is found in the original specification, e.g., at pages 5-6. No new matter is added by these amendments.

The following remarks are in response to the Office Action mailed June 4, 2007 ("the Office Action").

Applicants acknowledge withdrawal of the rejection of claims 1-18 and 21 under 35 U.S.C. § 112, second paragraph, the withdrawal of the rejection of claims 1-18 and 21 under 35 U.S.C. § 102(b), as anticipated by Singh et al. (WO 01/00662), and the withdrawal of the rejection of claims 1-18 and 21 under 35 U.S.C. § 102(e), as anticipated by Khodadoust et al. (US Pat. Pub. No. 20030022170).

Claim Objections

Claims 1-18 and 21 were objected to because they recite non-elected species (e.g., SEQ ID NOs.:1 and 2). Upon allowance of a generic claim, Applicants will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim. MPEP § 809.02(a).

Rejections under 35 U.S.C. § 112, first paragraph

Claims 1-18, 21, 24, 25, and 27 were rejected as allegedly lacking enablement. The Office Action acknowledged that the specification is enabling for " a method of treating a bone

condition characterized by too little bone formation or for increasing or maintaining bone density or for stimulating osteoblast growth comprising administration of an FGF-8 agonist polypeptide having at least 95% sequence identity to SEQ ID NO:1, 2, or 3." However, it stated that the specification does not reasonably provide enablement "for administration of FGF-8 variants, fragments or agonists as broadly claimed."

The claims, as amended, recite methods of using FGF-8 and FGF-8 agonists, wherein the FGF-8 agonist comprises an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 1, 2, or 3. The term "or a fragment thereof comprising at least 10 amino acids of the sequence" has been deleted from the claims. Therefore, the comments in the Office Action regarding the "enormous number of non-functional fragments" are inapplicable. Claims 21, 26 and 27, as amended, and claim 23, are of a scope acknowledged as enabled in the Office Action. Claims 1, 5-7, and 12, as amended, and claims 2 and 8, are also of a scope acknowledged as enabled by statements in the Office Action, but which were included in the rejection. Applicants request reconsideration of these claims in view of the amendments and the following remarks.

In the Office Action mailed October 18, 2006, the Examiner cited Blunt et al. (*J. Biol. Chem.*, 272(6): 3733-3738, 1997; "Blunt") as evidence of lack of enablement for FGF-8 variants, and in response Applicants noted that Blunt does not report the effects of FGF-8 or FGF-8 variants on osteoblasts or osteoclasts. The Office Action stated that "the Examiner cited this reference to demonstrate that even FGF-8 analogs are not all capable of behaving in the same way; the reference need not teach the effect on osteoblasts and osteoclasts to be relevant, because the claims recite open language" (page 6). Applicants disagree that the information in Blunt is necessarily applicable to the present claims, because Blunt studied the effects of FGF-8 isoforms on a pro-B cell line, not in osteoblasts or osteoclasts. The fact that the present claims recite open language regarding FGF-8 does not render Blunt more applicable, as alleged.

Even so, Blunt shows that multiple FGF-8 isoforms do, in fact, share the ability to activate certain receptors. For example, Blunt reported that FGF-8b, FGF-8c, FGF-8d, FGF-8e, FGF-8f, and FGF-8g isoforms induce mitogenesis in BaF3 cells expressing FGFR3c receptors or FGFR4 receptors (Blunt, page 3735, right column, first full paragraph). There is variation within this genus of FGF-8 isoforms that is mitogenic for cells expressing FGFR3c and FGFR4 (see

Blunt, Fig. 1); some isoforms differ by the presence or absence of an entire exon. The authors of the reference reported that "the multiple FGF-8 isoforms are functionally redundant and function to signal in paracrine (epithelial to mesenchymal) contexts" (Blunt, abstract, last sentence). Thus, Blunt shows that variant isoforms are functionally redundant in some contexts. It does not show that multiple FGF-8 analogs cannot all behave the same way, as alleged in the Office Action.

The Office Action stated:

> [C]laims reading on significant numbers of inoperative embodiments would render claims non-enabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative (page 6).

Applicants submit that the claims do not read on significant numbers of inoperative embodiments. In addition, the experimentation required to make and use an FGF-8 agonist that is at least 95% identical to SEQ ID NO:1, 2, or 3, is not undue. The specification describes multiple forms of FGF-8 (e.g., at pages 2-3), functional properties of FGF-8 agonists (e.g., at page 5, lines 6-9), and biological assays for the agonists (e.g., Examples 1-3). The Office Action stated that "the claims encompass treatment, and not merely 'screening an agonist'...making and testing drugs is not the standard for enablement" (page 7). Applicants note that specification provides evidence of therapeutic utility for FGF-8. For example, it demonstrates that FGF-8 stimulates osteoblast proliferation and inhibits osteoclast formation (see Examples 1 and 2). The breadth of the claims regarding this utility is not unreasonable. Using the examples provided and the guidance in the specification there is no reason why one of ordinary skill in the art could not practice the full scope of the methods claimed. Applicants respectfully request withdrawal of the rejection of claims 1-18 and 21, as lacking enablement.

CONCLUSION

Allowance of the claims is respectfully requested in view of the above remarks. A Petition for Extension of Time, Notice of Appeal, and required fees are being filed herewith. Please apply any other charges or credits to deposit account 06-1050, referencing attorney docket no. 08987-009001.

Respectfully submitted,

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